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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,282	08/22/2006	Eric E. Schadt	ROSA134255	2454
26389	7590	03/11/2011	EXAMINER	
CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC 1420 FIFTH AVENUE SUITE 2800 SEATTLE, WA 98101-2347			SMITH, CAROLYN L	
			ART UNIT	PAPER NUMBER
			1631	
			NOTIFICATION DATE	DELIVERY MODE
			03/11/2011	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

[efiling@cojk.com](mailto:efiling@cojk.com)

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/567,282	SCHADT ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Carolyn Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 12 October 2010 and 07 January 2011.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 108-134, 137-139, 142-160, 211-235 and 297-318 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 108-134, 137-139, 142-160, 211-235 and 297-318 is/are rejected.
- 7) Claim(s) 211, 297, and 298 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|  | 6) <input type="checkbox"/> Other: _____ .                        |

## **DETAILED ACTION**

Applicant's amendments and remarks, filed 10/12/10 and 1/7/11, are acknowledged.

Amended claims 108, 109, 110, 129, 132, 152, 156, 159, 160, 211, 223, 232 and cancelled claims 1-107, 135-136, 140-141, 161-210, 236-296 are acknowledged.

Applicant's arguments, filed 10/12/10, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims herein under examination are 108-134, 137-139, 142-160, 211-235, and 297-318.

### **Claim Objections**

Claims 211, 297, and 298 are objected to because of the following informalities:

Claims 211, 297, and 298 recite "organisms" and "organsims" which are misspelled.

Appropriate correction is required.

**Claims Rejected Under 35 U.S.C. § 112, Second Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 119-121 and 304 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The term "associated with" in claims 119, 120, and 304 is a relative term which renders the claim indefinite. The term "associated with" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what Applicant intends this phrase to mean. Clarification of this issue via clearer claim wording is requested.

Claim 121 is also rejected due to its dependency from claim 120. This rejection is maintained.

Applicant argues "associated with" is understood by those of skill in the art in view of the specification that describes association studies which test whether a disease and an allele show correlated occurrence within a population. This statement is found unpersuasive as the claims merely state "associated with" and it is unclear what Applicant intends this phrase to mean. It is unclear if Applicant intends this phrase to mean. It is unclear if "associated with" means it is causative, if it is resulting from, if it is placed next to each other in a table, or some other scenario.

**Claim Rejections – 35 USC §102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 108-134, 137-139, 142-160, 211-235, and 297-318 are rejected under 35 U.S.C. 102(e) as being anticipated by Schadt et al. (US 2006/0111849). This rejection is maintained and reiterated for reasons of record.

Schadt et al. disclose a method, computer product, and system of determining whether a first trait is causal for a second trait in a plurality of organisms of a species (abstract, 0092, 0248, 0286, claim 54) comprising identifying one or more loci that is a site of colocalization for quantitative trait loci for first and second traits (abstract, 0017-0019, 0027, 0086, 0280, 0287, 0388), testing each locus for genetic variation (0003, 0088-0092, 0095, 0127), wherein correlation determines a trait to be causal for a second trait (0018, 0074, 0084-0085, 0092, 0093, 0111, 0127, 0242-0249, 0286-0287, 0292-0295), as stated in instant claims 108, 159, 160.

Schadt et al. disclose determining a QTL using a first and second QTL analysis (abstract), as stated in instant claims 109-110. Schadt et al. disclose colocalization within 1 cM (0285, 0303), as stated in instant claims 111-112, 147-148, 215-216. Schadt et al. disclose a predetermined set of individuals and strains and organisms derived from strains (0037, 0095, 0160, 0318-0319,

0370-0371, 0384) and organisms derived from crossing or F2 mating (0034, 0063, claim 11), as stated in instant claims 113-118, 120, 122, 123. Schadt et al. disclose a phenotype associated with human disease, such as obesity, diabetes, etc. (0017, 0024), as stated in instant claims 119-121. Schadt et al. disclose a plurality of one or more organisms (abstract, 0017), as stated in instant claims 124-127, 217-219. Schadt et al. disclose abundance levels of cellular constituents, including RNA (0193, 0197-0200), as stated in instant claims 128, 130, 131, 307, 316. Schadt et al. disclose normalization (claim 12), as stated in instant claim 129. Schadt et al. disclose contacting a gene transcript array with RNA to measure abundance (0193-0200), as stated in instant claim 132. Schadt et al. disclose testing linkage, advancing the position, and repeating steps, and a statistical lod score greater than 4.0 (0022-0023), as stated in instant claims 133-134, 137-139, 142-143. Schadt et al. disclose quantitative measurements that are amounts of concentration of cellular constituents (0319), as stated in instant claims 144-145. Schadt et al. disclose humans (0059), as stated in instant claims 146, 220. Schadt et al. disclose two loci (0075), as stated in instant claim 149. Schadt et al. disclose colocalization and satisfying or failing a pleiotropy test (0085-0088, 0137) and null and alternative hypotheses (0114, 0215, 0255), as stated in instant claims 150-151, 230-231. Schadt et al. disclose the model equations of instant claims 152-154 and 232-234 (0282-0283) and maximum likelihood analysis with by maximizing loglikelihood (0284), as stated in instant claims 155 and 235. Schadt et al. disclose a method, computer product, and system of determining whether a first trait is causal for a second trait in a plurality of organisms of a species (abstract, 0092, 0248, claim 54) comprising identifying one or more loci that is a site of colocalization for quantitative trait loci for first and second traits (abstract, 0017-0019, 0027, 0086, 0280, 0287, 0388), quantifying a first and second

coefficients of determination between genetic variations (0003, 0076-0092, 0095, 0127), wherein a trait to be causal for a second trait based on the coefficients (0018, 0074, 0080-0085, 0093, 0111, 0127, 0236, 0242-0249, 0282-0287, 0290-0295, 0367, 0402-0403), as stated in instant claims 211, 297-298. Schadt et al. disclose using thresholds, including less than 0.10 and less than 0.05 (0087, 0236, Figure 6), as stated in instant claims 212-214. Schadt et al. disclose a complex trait (claim 42), as stated in instant claim 221. Schadt et al. disclose a complex trait that is characterized by an allele that exhibits incomplete penetrance in said species (claim 43) and is a contracted disease (claim 44), as stated in instant claims 222-223, 299-301, 308-309, 310. Schadt et al. disclose the complex trait arises when a gene is mutated (claim 45), simultaneous presence of mutations (claim 46), does not exhibit Mendelian recessive or dominant inheritance (claim 48), is asthma, ataxia telangiectasia, etc. (claim 49), associated with a high frequency of disease-causing alleles (claim 47), colocalize within 40cM, 10cM (claims 50, 52), as stated in instant claims 224-229, 302-306, 311-315. Schadt et al. disclose a first trait is an abundance level with an eQTL and a cQTL (abstract, claim 14), as stated in instant claims 317 and 318.

Thus, Schadt et al. anticipate the instant invention.

Applicant summarizes claim amendments and Schadt et al. Applicant argues Schadt et al. do not teach methods for determining causality as claimed. This statement is found unconvincing as Schadt et al. disclose using QTL (quantitative trait loci) and probe location information to piece together causal pathways as well as a result of a set of pathway groups consisting of genes and causal information that indicates the exact relationship of genes in the pathway (or of a partial set of genes in the pathway) (0018, 0092, 0292-0295). Applicant argues

Schadt et al. do not disclose step B or the wherein clause of instant claim 108. This statement is found unpersuasive as Schadt et al. disclose a method, computer product, and system of determining whether a first trait is causal for a second trait in a plurality of organisms of a species (abstract, 0092, 0248, claim 54) comprising identifying one or more loci that is a site of colocalization for quantitative trait loci for first and second traits (abstract, 0017-0019, 0027, 0086, 0280, 0287, 0388), testing each locus for genetic variation (0003, 0088-0092, 0095, 0127), wherein correlation determines a trait to be causal for a second trait (0018, 0074, 0084-0085, 0092, 0093, 0111, 0127, 0242-0249, 0286-0287, 0292-0295). Applicant argues that Schadt et al. do not disclose step C of instant claims 211 and 297. This statement is found unpersuasive as Schadt et al. disclose a method, computer product, and system of determining whether a first trait is causal for a second trait in a plurality of organisms of a species (abstract, 0092, 0248, claim 54) comprising identifying one or more loci that is a site of colocalization for quantitative trait loci for first and second traits (abstract, 0017-0019, 0027, 0086, 0280, 0287, 0388), quantifying a first and second coefficients of determination between genetic variations (0003, 0076-0092, 0095, 0127), wherein a trait to be causal for a second trait based on the coefficients (0018, 0074-0089 [QTL interaction maps provide info on which QTLs are linked and elucidate pathways that affect complex traits; QTL interacting with another QTL; plurality of correlation coefficients is computed; associating genes with traits; consider multiple traits simultaneously and determine if the traits are linked to each other], 0092 [piece together causal pathways, causal information indicating exact relationship of genes in pathway], 0093, 0111, 0127, 0233 [lod score representing chance of a loci being linked to a trait], 0236, 0242-0249, 0275-0290 [look at variation and determine if cQTL and eQTL genetically interact with each other and use null and

alternative hypotheses], 0289-0295 [conditioning; causal factor], 0367, 0402-0403 [correlation coefficients of a gene regulating traits linked to a locus and causative candidates for linkage activity at the locus], claims 258-262 [testing for pleiotropy comparing a null hypothesis involving two traits and a locus in a plurality of organisms with some conditions that are or are other than zero]). It is noted that “trait” and “coefficient” have been interpreted broadly and reasonably. Applicant argues Schadt et al. do not qualify as prior art under 35 USC 103(a) in view of 35 USC 103(c)(1). While this statement is acknowledged, it is noted that no 35 USC 103 rejection was made.

### **Conclusion**

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. If you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, please call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on (571) 272-0720.

March 7, 2011

/Carolyn Smith/  
Primary Examiner  
AU 1631